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Anatomic and Hemodynamic Considerations Influencing the Efficiency of Retrograde Cardioplegia

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One of the major issues raised by cardiac surgical procedures requiring cardiopulmonary bypass is the question of myocardial protection. The preferred route for the administration of cardioplegia is controversial. A number of studies show the beneficial effects of retrograde cardioplegia but some demonstrate only partial or poor myocardial protection. This paper reviews the anatomy and anatomic variations of the coronary sinus, the coronary sinus orifice and cardiac veins, and the major systemic venous drainage, all of which may affect the distribution of retrograde cardioplegia.

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Pratt [1] suggested in 1898 that oxygenated blood could be supplied to an ischemic myocardium through the coronary venous system. In 1956, Lillehei and colleagues [2] used retrograde coronary sinus perfusion to protect the heart during an aortic valve operation. Since then, retrograde coronary sinus cardioplegia (RCP) has gained widespread use as a method of myocardial protection in a broad range of cardiac procedures. The advantages of RCP are (1) the provision of a relatively uniform distribution of cardioplegia even in the presence of severe coronary artery disease which can alter the distribution of antegrade cardioplegia [3, 4] (the coronary sinus venous system is a dense vascular network that is not affected by arteriosclerosis or extensive disease in the coronary arterial system, and in hearts with coronary artery disease there is a richer, more uniform venous network in the subendocardial zone of both ventricles) [5, 6]; (2) it is effective in the presence of aortic regurgitation or an open aortic root and where there is no risk of coronary ostial injury [7]; (3) in certain clinical situations, such as reoperative coronary artery bypass surgery, antegrade cardioplegia is associated with a high risk of atheromatous embolization from patent grafts, whereas RCP may flush distal emboli from the arterial system [8]; (4) RCP may be an effective method for treating coronary air embolism [9]; and (5) it can be given without interrupting the surgical procedure. Despite these benefits, however, the efficacy and safety of using RCP alone for myocardial protection remains controversial, especially in relation to the protection of the right ventricle [10–13].

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Venous Anatomy of the Heart

There are three venous systems that drain the heart: the coronary sinus, the anterior cardiac veins, and the venae cordis minimae [14].

The coronary sinus opens into the right atrium between the opening of the inferior vena cava and the tricuspid orifice. It returns blood to the right atrium from nearly all regions of the heart, including the septa, and accounts for 75% of the coronary venous circulation (Fig 1). Owing to the high left ventricular cavity pressure, the coronary sinus has evolved to provide a low-pressure drainage outlet for the left heart and ventricular septum. The anterior region of the right ventricle and small variable parts of both atria are not drained by the coronary sinus.

The anterior cardiac veins drain an anterior region of the right ventricle and a region around the right cardiac border, ending in the right atrium at the atrioventricular groove. The largest of these veins accompanies the acute marginal artery and is called the small cardiac vein. The venae cordis minimae (Thebesius' veins) open directly into the right atrium and ventricle, to a lesser extent into the left atrium, and occasionally into the left ventricle.

Many anomalies of the venous anatomy of the heart have been identified. These include anomalies of the coronary sinus and veins. All these anomalies may impact on the distribution of RCP.

Anomalies of the Coronary Sinus

Coronary sinus anomalies can occur without any effect on cardiac function and without clinical symptoms or signs. However, they can still affect the distribution of the RCP. Coronary sinus anomalies have been classified into five types [15, 16]. (1) An absent coronary sinus is always associated with a persistent left superior vena cava (PLSVC) connecting to the left atrium. (2) A hypoplastic

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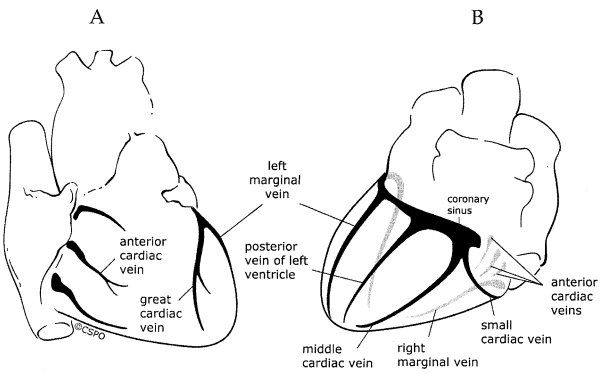

Fig 1. Venous drainage of the heart: (A) anterior view; (B) posterior view. (Adapted from Buxton B, Smith J, Kainer M, Ruengsakulrach P. Basic surgical techniques. In: Buxton B, Frazier OH, Westaby S, eds. Ischemic heart disease surgical management. London: Mosby, 1999:185.)

coronary sinus occurs when one or more of the cardiac veins drain directly into the atria. (3) Atresia or stenosis of the coronary sinus ostium may occur alone or with associated cardiac anomalies. In this anomaly, the coronary veins drain by an alternative pathway either through a PLSVC (retrograde drainage) and the innominate vein, a window to the left atrium, multiple connections through Thebesius' veins to the atria, or a levoatriocardinal vein connecting the coronary sinus and the left atrium. (4) Enlargement of the coronary sinus can be divided into two groups: *without left-to-right shunt*, a group that includes PLSVC (the most common), hepatic vein draining into coronary sinus, and left inferior vena cava (IVC) draining into the coronary sinus; and *with left-to-right shunt*, which includes anomalous pulmonary vein or veins that drain into the coronary sinus, coronary artery-coronary sinus fistula, and coronary sinus-left atrium window. (5) The "unroofed" coronary sinus anomaly is associated with a deficiency of the common wall between the coronary sinus and left atrium; it may be a partial defect where a circular or elliptical fenestration is present in the midportion of the roof of the coronary sinus. Alternatively, the coronary sinus may be fully unroofed resulting in a complete communication between the coronary sinus and the left atrium. Most cases are associated with a PLSVC [17].

Persistent Left Superior Vena Cava

In normal embryonic development, the primitive sinus venosus receives the anterior cardinal veins from the upper part of the body and the posterior cardinal veins from the posterior part of the body. In the seventh week of gestation, the superior and inferior vena cava replace the cardinal system. The left horn of the sinus venosus regresses to become the coronary sinus and receives only the vestigial oblique vein of Marshall, a remnant of the left anterior cardinal vein and the coronary venous drainage (Fig 2).

PLSVC, the most common anomaly of the major veins, is a result of a residual left anterior cardinal vein. It occurs in 0.1% to 0.3% of the general population. In patients with a congenital cardiac malformation, the prevalence of PLSVC is 3% to 8%, and up to 40% when such patients have abnormal situs [18–21]. There is a significant positive correlation between PLSVC and the congenital anomalies of mitral atresia, atrioventricular septal defects and cor triatriatum [21]. A PLSVC originates from the junction of the left innominate vein and the left jugular vein. It descends vertically and enters the pericardial cavity at the posterior atrioventricular groove, continuing in most cases to the right atrium through the coronary sinus. More than 90% of cases of PLSVC drain through a coronary sinus. The rest drain into the coronary sinus through a window into the left atrium, directly into the left atrium or into the left pulmonary vein (Fig 3) [15]. In 60% of cases, the innominate vein bridges the two superior venae cavae; in the other 40%, the cavae drain the right and left brachiocephalic regions separately. If there is no innominate vein the PLSVC must persist; however, the converse is not true. A PLSVC with an absent right superior vena cava is found in 14% of cases [22].

When a PLSVC is encountered, several questions need to be answered: Is there a right superior vena cava? Is the innominate vein present? Is the PLSVC associated with any other cardiac malformations? Where does the PLSVC drain? And does the surgery involve the right atrium?

In diagnostic terms, a preoperative electrocardiogram (ECG) may show a leftward deviation of the P-wave axis or associated conduction anomalies while a chest Roentgenogram sometimes reveals the PLSVC as an extra structure in the area of the aortic knob and upper mediastinum. Preoperative or intraoperative transesophageal echocardiography (TEE) may show an unusual round vascular object lying beside the left atrioventricular junction on a four-chamber or a two-chamber view [23, 24]. Associated cardiac anomalies can also be identified by TEE. Another diagnostic test that can be used to confirm the presence of a PLSVC is contrast echocardiography [25]. During surgery, with the retrograde cannula in the correct position, a low coronary sinus pressure, absence of complete arrest, and a dilated coronary sinus with or without an innominate vein, may also be suggestive of a PLSVC.

Techniques of cardiopulmonary bypass, myocardial

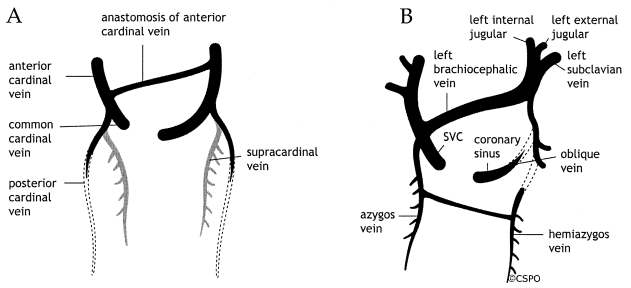

*Fig 2. The development of the major thoracic veins: (A) at 7 weeks; (B) full term. (*SVC = *superior vena cava.) (Adapted from Sadler TW. Langman's medical embryology. 8th ed. Baltimore: Lippincott, Williams & Wilkins, 2000:249.*

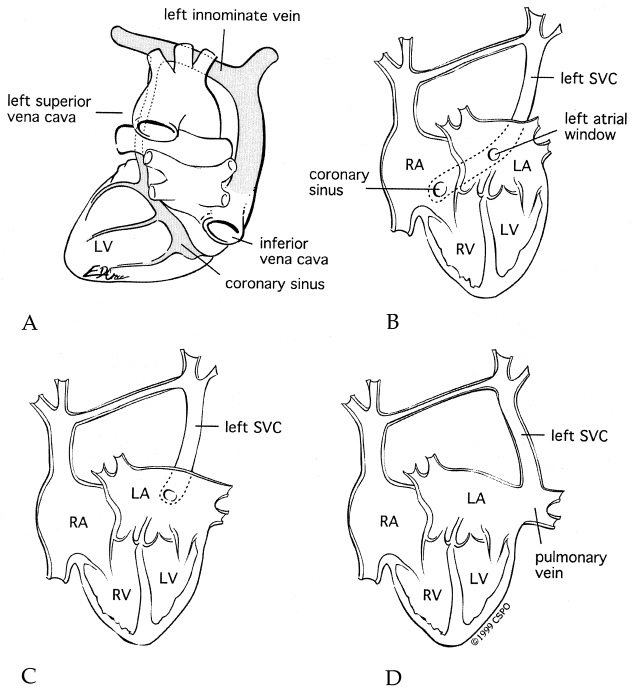

Fig 3. Persistent left superior vena cava (PLSVC). (A) PLSVC drains through the coronary sinus into the right atrium (RA). *The sizes of PLSVC and left brachiocephalic vein are inversely proportional. (B) PLSVC drains into the coronary sinus and a window into the left atrium. (C) PLSVC drains into the left atrium. (D) PLSVC drains into the left pulmonary veins.* (SVC = *superior vena cava;* LV = *left ventricle;* LA = *left atrium;* RV = *right ventricle;* RA = *right atrium.) (Adapted from Mantini E, Grondin CM, Lillehei W, Edwards JE. Congenital anomalies involving the coronary sinus. Circulation 1966;33:317–27.)*

protection, and surgery are dictated by the nature of the complex cardiac anomalies associated with a PLSVC. For instance, a PLSVC that drains venous blood from the left internal jugular vein and left arm through the coronary sinus to the right atrium can be temporarily occluded to avoid cardioplegic solution shunting to these veins and also to prevent cerebral and left arm edema. The orifice of the dilated coronary sinus may require compression to prevent runoff into the right atrium of the cardioplegia during retrograde infusion [26]. If the surgical procedure involves the right atrium, the PLSVC should be cannulated for venous drainage.

Variations of the Coronary Veins

Variations of the coronary veins, which are much more common than variations of the arteries, may cause nonhomogenous distribution of RCP and result in inadequate myocardial protection.

In 1987, Ludinghausen [27] examined 350 hearts macroscopically and defined five groups of coronary vein variations (Fig 4). Of concern when using RCP are the variations shown in Figure 4D and E (13% of coronary vein variations) in which large areas of the left ventricle are not directly drained by the coronary sinus.

In relation to the blood supply of the human interventricular septum, Hammond and Austen [28] suggest that, while it has four or five septal arteries, the septum has no accompanying veins so that drainage occurs almost exclusively into the ventricular lumina. In all likelihood, there is some degree of venous drainage accompanying the arterial circulation of the ventricular septum. Nevertheless, the venous anatomy of this area is limited, suggesting that the septum is likely to be poorly perfused during RCP.

The middle cardiac vein, which may drain blood from some parts of the interventricular septum, opens into the coronary sinus very close to its ostium. The mean distance between the coronary sinus ostium and the middle cardiac vein is 1.7 ± 0.6 mm in adults. Accordingly, it is not possible to secure the RCP balloon in place in the coronary sinus without occluding the openings of these veins. However, this vein can be perfused in a retrograde direction through widespread anastomoses at all levels of the cardiac venous circulation [29, 30].

Farge and colleagues [31] analyzed the distribution of flow during RCP in human hearts (from cadavers) using two different techniques of coronary sinus cannulation: internal occlusion of the coronary sinus by balloon inflation and external occlusion by restricting the orifice of the coronary sinus near its termination with a pursestring suture. With intraluminal inflation, regardless of balloon position, filling by venovenous anastomosis between the great cardiac vein and the middle cardiac vein did not consistently perfuse the interventricular septum. External occlusion of the coronary sinus at its termination

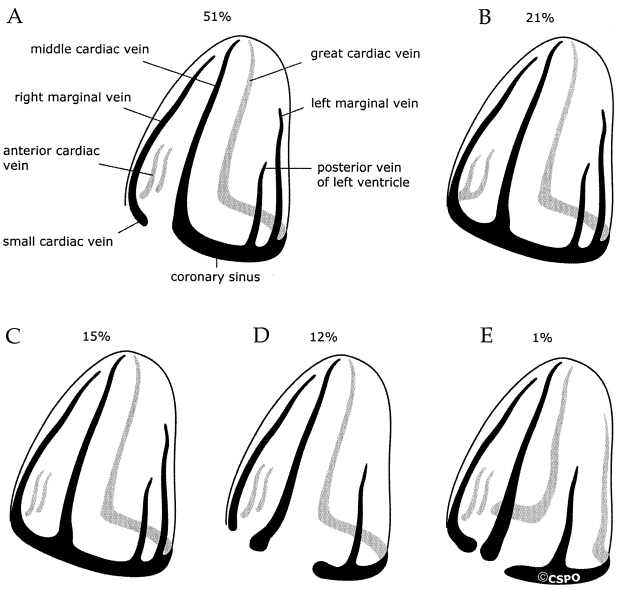

Fig 4. Posterior aspect of the heart. Variations in the distribution pattern of the coronary sinus and venous myocardial drainage: (A) anterior and small cardiac veins enter the right atrium; (B) all major cardiac veins enter the coronary sinus; (C) anterior cardiac veins enter the right atrium; (D) only great cardiac vein and posterior vein of left ventricle enter the coronary sinus; (E) only veins of the lateral wall of left ventricle enter coronary sinus. (Adapted from Ludinghausen [27].)

resulted in simultaneous injections of all venous channels and most of the septum was well perfused. Nevertheless, the right ventricular free wall was not adequately perfused with either of these techniques [31].

This problem can be avoided, however, by careful observation of the distribution of cardioplegia in the middle cardiac vein as well as closely monitoring the coronary sinus pressure during RCP. If the middle cardiac vein is not perfused after RCP, and other veins are well filled, the position of the catheter needs to be checked and repositioned. The balloon of the catheter may be placed too far in the coronary sinus or the sinus may be too short. If the balloon is too far in, it can be retracted towards the orifice of the coronary sinus. However, if the coronary sinus is short, the RCP catheter is easily dislodged. It can be secured with a pursestring suture through the right atrium in tricuspid or mitral valve surgery or through an externally placed snare around the coronary sinus orifice on the inferior aspect of the heart. Furthermore, manual external compression can be applied to prevent leakage of the cardioplegic solution. Some investigators have suggested improving left ventricular distribution by routinely occluding the orifice of the middle cardiac vein with a special extended balloon catheter or by placing a clamp on the origin of the middle cardiac vein [32–34]. In this latter case, the middle cardiac vein will be filled by collateral veins. If the middle cardiac vein does not fill by manipulation of the coronary sinus catheter, antegrade cardioplegia should be given in combination with RCP.

Anomalies of the Coronary Sinus Opening and Coronary Vein Valves

The coronary sinus opening is guarded by an endocardial fold—the semilunar valve of the coronary sinus (Thebesian valve). The valve at the orifice of the coronary sinus varies in size and form.

Hellerstein and Orbison [35] studied 150 human hearts at autopsy. There were six variations of the Thebesian valve (1) absent, 14.7%; (2) small and crescentric, 38%; (3) large and covering the entire orifice of the coronary sinus, 30.7%; (4) bars and bands, 5.3%; (5) threads and networks, 5.3%; and (6) common Eustachian and Thebesian valves, 6%. In another study of the clinical anatomy of the cardiac veins, the openings of the cardiac veins (the great cardiac vein, the left marginal vein, the posterior vein of the left ventricle, and the middle cardiac vein) into the coronary sinus were found to have completely closed funnel valves in 26% of patients while there were no real valves in approximately 45% of cases [27].

When a competent valve does exist, the pressure induced by retrograde infusion must be raised sufficiently to distend the coronary sinus before the valve can open. Tributary veins will then suddenly fill during RCP [36]. The pressure gradient at which the valve opens varies depending on the flow rate of retrograde perfusate. In general, the coronary sinus pressure is limited to 40 mm Hg to prevent coronary sinus injury, peripheral vascular edema and hemorrhage. However, a recent study showed that in the vented arrested heart the coronary sinus pressure can be increased to up to 120 mm Hg without extravasation of blood into the myocardium [37]. Cardioplegic safety systems are available that limit the perfusion pressure (The Medtronic CSS Cardioplegic Safety System; Medtronic Bio-Medicus Inc, Eden Prairie, MN). Adequate flow is also dependent on the temperature and cardiac muscle mass; for example, with retrograde warm cardioplegia, the flow rate should be delivered at a minimum of 200 mL/min [38] whereas in patients with left ventricular hypertrophy the RCP flow should be increased to 250 to 300 mL/min.

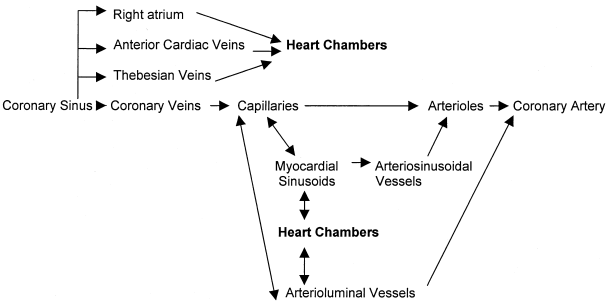

Fig 5. Pathways of retrograde cardioplegia. (Adapted from Wearn JT, Mettier SR, Klumpp TG, Zschiesche LJ. The nature of the vascular communications between the coronary arteries and the chambers of the heart. Am Heart J 1933;9:143–59.)

Hemodynamics and Nutritive Flow of Retrograde Cardioplegia

Physiologically, venous blood is forced out of the cardiac venous system and into the right atrium by the beating of the heart through the Thebesius' veins and the coronary sinus. During cardiac contraction, the natural flow within the coronary venous system is contrary to the intended flow of retrograde perfusion. RCP in a working heart can therefore generate high venous pressures. Once the heart is arrested, however, the impedance provided by the natural flow of venous blood can be easily overcome. For this reason, antegrade cardioplegia should be used for the induction of cardiac arrest. However, antegrade cardioplegia does not completely perfuse all available capillary beds, even in patients with normal coronary arteries. The presence of precapillary and postcapillary shunts may result in antegrade and retrograde cardioplegia supplying different vascular beds (Fig 5). For example, in an arrested heart, the Thebesius' veins can serve as low-resistance conduits draining into lower pressure chambers and diverting RCP away from venules and capillaries to the right ventricle. Furthermore, antegrade cardioplegia provides nutritive flow to the right ventricle when anterior cardiac veins are not developed or not connected to the coronary sinus. These hemodynamics and physiologic processes suggest that a combination of retrograde and antegrade cardioplegia (simultaneous or sequential) should be used.

In an experimental animal study, total cardiac nutritive flow averaged 70% of flow delivered during RCP when both the left anterior descending artery (LAD) and cir-

cumflex coronary artery were open, falling to 61% when the LAD was occluded adjacent to the first diagonal branch [39]. Retrograde capillary flow through the interventricular septum was low regardless of whether the LAD was patent or occluded. However, myocardial flow into the septum was preferentially through the endocardium, which is more extensively perfused by retrograde perfusion than antegrade perfusion even with the LAD occluded. The lowest nutritive flow occurred in the right ventricular free wall. However, there were some concerns about anatomical differences between the human and the canine heart, which may explain the poor right ventricular protection in this study. A study of coronary effluent following RCP in explanted human hearts from transplant recipients with idiopathic cardiomyopathy showed that 67.2% of RCP was shunted through the Thebesius' veins, thereby bypassing the microvasculature. 29.3% and 3.5% of the cardioplegia traversing the myocardium emerged from the left and right coronary arteries, respectively [40]. The cardioplegia that shunted to the heart chambers, however, was partly nutritive flow through capillaries, myocardial sinusoids and arterioluminal vessels (Fig 5) [41]. Sinusoids are sparse, irregular shaped channels with an endothelial lining. They act as inefficient capillaries in which the blood only partially desaturates before it is drained into the lumen of the left ventricle.

In clinical practice, the route of cardioplegic perfusion remains controversial. In 1992, for example, 4,393 American board-certified thoracic surgeons were surveyed; 1,413 responded (32.2%) and the results were published in 1995 [42]. The methods used for cardioplegic delivery were a combination of antegrade and retrograde (60%), antegrade (36%), and retrograde (4%). Most centers reported good results irrespective of the method of delivery. However, at the same time, these apparently uniform results were confounded by other important factors that may affect the efficacy of cardioplegia including technique of cannulation, cardioplegic solution composition, temperature of solution, perfusion flow rate, and time of infusion.

Recommendations

The widespread variations in the venous drainage of the heart suggest that a combination of intermittent antegrade and nearly continuous retrograde blood cardioplegia may provide superior myocardial protection when coronary obstructions interrupt and limit cardioplegic delivery [42–50].

RCP should be delivered in conjunction with a pressure-limiting system to prevent damage or rupture of the coronary sinus. The distribution of RCP should be assessed by examining the middle cardiac vein and anterior cardiac veins during perfusion because RCP may not perfuse all of the right ventricular free wall and septum. Distribution of RCP to the free wall of the right ventricle is often poor because there is no direct communication between the coronary sinus and anterior cardiac veins. This may be a problem in patients with inadequate venous collaterals or right ventricular dysfunction, if the RCP catheter is placed in too far to the left, or if the operation is especially prolonged. If these tributaries do not fill or become oxygenated after infusion, antegrade cardioplegia should be given in addition to retrograde perfusion because antegrade cardioplegia is relatively well distributed to both the left and right ventricles in the absence of coronary artery disease.

Our policy is to give the first dose of blood-based cardioplegia in antegrade and retrograde directions sequentially. Other surgeons prefer to use antegrade and retrograde cardioplegia simultaneously and have reported improved results despite the potential risk of myocardial edema as a result of increased coronary sinus pressure [51–53]. Subsequent doses are given by a retrograde route to decrease aortic occlusion time and avoid the introduction of emboli, which may occur during antegrade cardioplegia, through the coronary arteries. However, in a case where the aortic occlusion time is expected to be long, or in a patient with an acutely ischemic myocardium or an acute myocardial infarction, the subsequent doses should be given by both an antegrade and retrograde route. Antegrade cardioplegia should be supplemented frequently to avoid irreversible muscle injury during normothermic ischemia, as there is some evidence that antegrade cardioplegia may be more effective than retrograde cardioplegia [49]. Supplemental antegrade cardioplegia, given by the aortic route down aortocoronary grafts is more efficient in patients with coronary artery disease because it perfuses grafted vessels, especially the right coronary artery. The last dose of cardioplegia is given retrogradely to remove air from the coronary arteries. In addition to the route of delivery, the temperature of the heart, the composition of the cardioplegia and the frequency of doses can all contribute to the clinical outcome.

Special Problems

1. Significant aortic regurgitation: our preferred route for the first dose of cardioplegia is antegrade combined with manual compression of the left ventricle to prevent regurgitation and dilatation until cardiac arrest and followed by RCP supplemented with direct coronary infusion after aortotomy.

2. Left ventricular hypertrophy: we recommend increasing the flow and frequency and decreasing the temperature of cardioplegia.

3. Acute myocardial infarction: the aortic cross clamp should be applied early. Antegrade cardioplegia is followed by continuous RCP to provide maximum myocardial protection and resuscitation in the presence of an acute occlusion.

4. Acute dissection: in Stanford type A aortic dissection, we use moderate to deep hypothermia. An aortic cross clamp may be applied during cooling or after ventricular fibrillation if the heart distends despite venting. Cardioplegia is induced by direct coronary cannulation or retrograde infusion.

5. Variants of the coronary sinus (ostial stricture or

stenotic valve): if a retrograde cardioplegic cannula cannot be inserted, antegrade cardioplegia is given alone.

6. Variants of the coronary venous anatomy: although coronary vein variations are common, major anomalies may be difficult to identify. To be sure that all areas of the heart are well perfused, antegrade and retrograde cardioplegia is used in all but the simplest procedures.

Conclusion

There are numerous variations of the coronary veins, coronary sinus, valves and systemic/pulmonary venous return systems, all of which may affect the degree of myocardial protection provided by retrograde cardioplegia. Major venous anomalies are usually detected preoperatively or, less frequently, during surgery. Although such anomalies are uncommon, when present they may profoundly affect the distribution of retrograde cardioplegia and will often necessitate the implementation of additional strategies in order to ensure adequate myocardial protection. As our review of the venous anatomy of the heart has demonstrated, it cannot be assumed that the heart is like a sponge and that all the venous channels interconnect freely. Thus, in order to prevent maldistribution of cardioplegia, an awareness of the anomalies and variations of the cardiac venous anatomy is essential. Accordingly, when there is evidence of a compromised cardiac vasculature, the use of both antegrade and retrograde cardioplegia is recommended.

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